REMARKS

Reconsideration is requested.

Claims 7 and 11-14 are pending. Claims 1-6 and 8-10 have been canceled, without prejudice. The claims have been amended, without prejudice, to advance prosecution. No new matter has been added.

The objection to claim 8 is moot in view of the above.

The Section 112, first paragraph "enablement", rejection of claims 7-14 stated on pages 2-7 of the Office Action dated November 30, 2007 is obviated by the above amendments. The Section 112, first paragraph "enablement", rejection of claims 7, 8 and 10-12 stated on pages 7-11 of the Office Action dated November 30, 2007 is obviated by the above amendments.

The claims define methods of using Etazolate which, as acknowledged by the Examiner, is supported by an enabling disclosure. Furthermore, the claims define methods of treatment of cognitive deficits in patients in need thereof. The application demonstrates that Etazolate improves the mnestic and cognitive properties in vivo in aged rats. More specifically, Example 5 of the application demonstrates in a well established and recognized in vivo model of cognitive deficits (the Aquatic labyrinth test) that Etazolate improves the mnestic and cognitive properties in aged rats. As discussed in the experimental section (Example 5):

> "This result indicates that etazolate improves the mnestic and cognitive properties dependent upon the hippocampus, making it possible to reduce the deficits of performance linked to age. This result qualifies etazolate for the treatment of cognitive problems linked to age such as Alzheimer's disease in particular. "

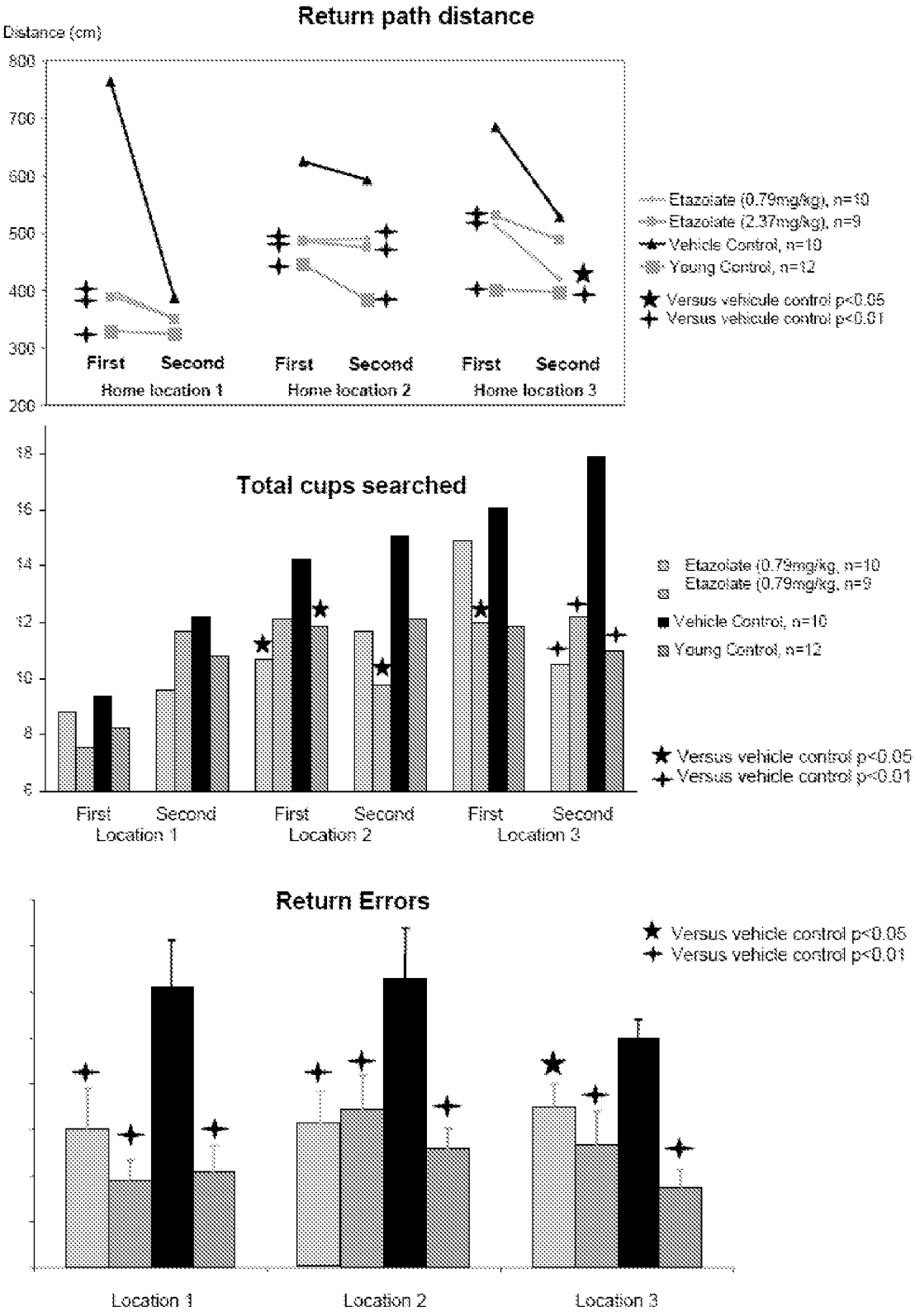
This unexpected property of Etazolate has also been confirmed by applicant in several series of additional experiments, detailed below, which show that: etazolate improves attention, learning capabilities and cognitive behaviour (Barnes test); and that etazolate reversed the deficit memory induced by scopolamine in rats.

In Barnes tests, a cognition model, using old rats, Etazolate improves attention, learning capabilities and cognitive behavior.

This test measures the short-term (working) memory independently of learning ability, as well as performance of a naturally occurring complex behavior, foraging and homing. Briefly, food-restricted rats are allowed to search for food pellets that have been placed in cups on a circular platform, and then return to their home box (located on the periphery of the circular search area) to either hoard or consume the pellets. Over several trials the rats learn which of the cups contain food pellets, and which of several identical boxes along the periphery is in fact their home box. Aged rats display several distinct deficits in performing this complex foraging/homing task, including disorientation and short-term memory impairment when their home box is placed in a new location.

In this study, Etazolate was administered at 0.79 or 2.37 mg/kg p.o. to aged male rats (> 29 months). Etazolate was able to restore aged rats ability to find their home as measured through a decrease in the return path distance and in the number of return errors. The Etazolate -treated animals became more efficient in their search strategy with fewer cups searched in comparison with aged vehicle rats. (Figure 1).

Figure 1: Return path distance, total cups searched and return errors to home Location 1, 2 and 3


Return path distance
Distance (cm)
800
700
600
500
400
300
200
First
Second
Home location 1
Home location 2
Home location 3
Etazolate (0.79mg/kg), n=10
Etazolate (2.37mg/kg), n=9
Vehicle Control, n=10
Young Control, n=12
Versus vehicle control p<0.05
Versus vehicle control p<0.01
Total cups searched
18
16
14
12
10
8
6
Location 1
Location 2
Location 3
Return Errors

In the following further study, Etazolate was investigated after IP administration in the scopolamine test. Scopolamine (0.5mg/kg) induced deficit memory in object recognition memory.

The first phase, i.e., training part, consisted of exposing the animals to two identical objects placed in symmetrical locations in a square plexiglass testing cage (16"x16") and allowed to explore the objects for 4 minutes or until they began grooming in the cage. Object recognition memory was tested 1 hr later with one of the original objects and a new, novel object. Animals were allowed to explore during testing for 3 minutes.

In the test phase, after administration of Etazolate or vehicle and scopolamine, object placement was identical to that during training, and the novel and familiar object were balanced across front/back cage locations to control for locational preferences. The time spent exploring the novel and familiar objects during testing was evaluated and a recognition index was calculated using the equation RI = Tn *100/(Tn+Tf) where Tn =time exploring the novel object and Tf = time exploring the familar object.

In this study, Etazolate was coded as compound A and was administered in dosages of 1 and 3 mg/kg, by IP (intraperitoneal route). The animals were administered vehicle or Etazolate 30 minutes prior to scopolamine (0.5 mg/kg) and 1 hr prior to training (scopolamine was therefore administered 30 minutes prior to training). The administration was performed in a volume of 1 ml/kg body weight. The test substances were dissolved in distilled water, which was the vehicle. For Etazolate the preparations

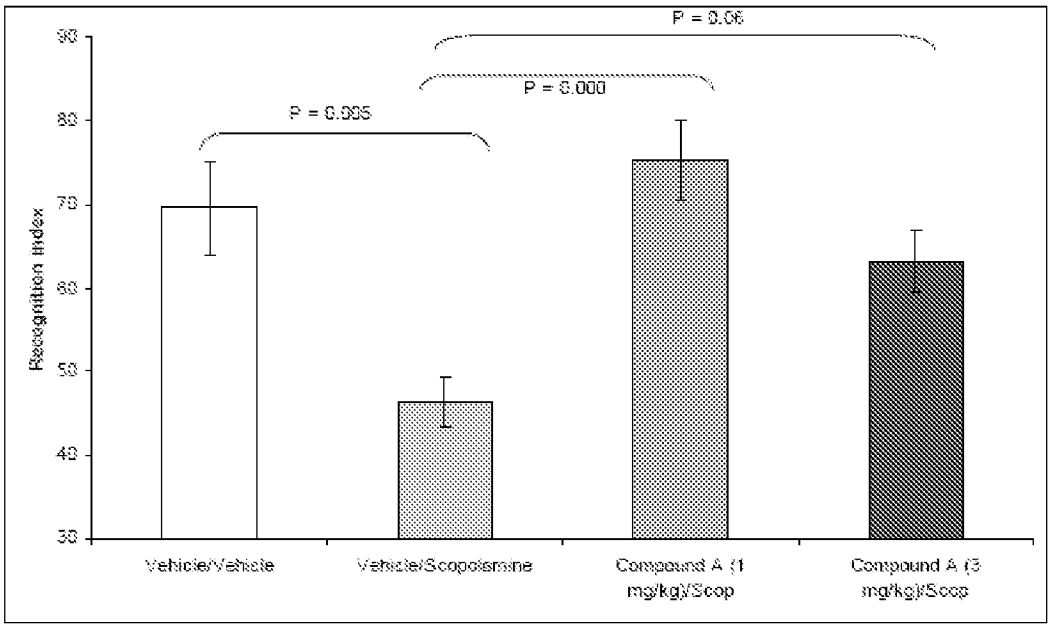
were made freshly for each day of administration and kept protected from light at 4°C during the period of administration.

This study used male sprague-dawley rats (weighing 150-200g) and rats were handled to comfort for 2 days before testing and were habituated to the test cages for 5 minutes the day before testing. On the test day, rats were brought to the test room 1 hr before the first injection. Data were analyzed using One way analysis of variance with Bonferroni post-hoc comparisons (using SPSS v 14.0 software).

The results of this study are summarized in the following table and figure:

Effects of Etazolate in scopolamine induced memory deficit in rats (n=8 per group)

Treatment	RI mean	sem
Vehicle/Vehicle	69,51	5,55
Vehicle/Scopolamine	46,32	2,96
Compound A (1 mg/kg)/Scop	75,30	4,81
Compound A (3 mg/kg)/Scop	63,21	3,65



There was a significant overall effect of treatment on recognition index scores [F(3,29) = 8.85, P = 0.000]. Bonferroni post-hoc comparisons indicated that vehicle+scopolamine treated rats had significantly lower RI scores relative to vehicle+vehicle rats (P = 0.005), whereas RI scores from rats treated with compound A+scopolamine (either dose) were not significantly different relative to vehicle (P = 1.000 for both comparisons). In addition, RI scores from rats treated with 1 mg/kg Compound A+scopolamine were significantly different than vehicle-scopolamine rats (P = 0.000) and a trend towards significance was observed between the 3 mg/kg Compound A+ scopolamine RI scores and the vehicle+scopolamine group (P = 0.06).

The applicants submit that the results of this study demonstrates that Etazolate reversed the deficit memory induced by scopolamine in rats.

The applicants believe the above, with the teachings and examples of the specification, demonstrate that one of ordinary skill in the art, using the present application and the generally advanced level of ordinary skill in the art, is able to make and use the claimed invention without undue experimentation. Withdrawal of the Section 112, first paragraph, rejections is requested.

To the extent not obviated by the above amendments, the Section 102 rejection of claims 7-12 over Bamdad (WO 01/78709 A2), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments. Bamdad et al relates to Tracazolate, and fails to teach each and every aspect of the claimed invention, which require use of Etazolate. Furthermore, the applicants submit that Bamdad et al fails to disclose or suggest the use of tracazolate for treating cognitive disorders, as presently claimed, but only refers to the treatment of degenerative disorders.

Withdrawal of the Section 102 rejection of claims 7-12 over Bamdad is requested.

To the extent not obviated by the above amendments, the Section 102 rejection of claims 13 and 14 over Ikhlef (U.S. Patent Application Publication No. 2003/0064374 A1), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

While Ikhlef et al. may relate to the treatment of Alzheimer disease, the reference does not disclose nor suggest the treatment of cognitive disorders, as presently claimed.

The study of the relationship between neuro-degeneration and cognitive deficits shows that there is no direct link between these distinct components of neuro-degeneration. Specifically, neuro-degenerative diseases are not necessarily associated to cognitive disorders. In contrast, while motility and coordination are signs of the pathology, cognitive disorders are, when they appear, a consequence of neuro-degeneration, and there is no demonstration of any quantitative correlation between neurogenesis and cognitive function. Accordingly, treating a neurodegenerative disorder does not mean nor imply treating, literally or inherently, a cognitive deficit, as presently claimed. These are two independent events having distinct mechanisms and cycles.

The instant invention shows and claims, for the first time, the therapeutic effect of etazolate on cognitive deficits. This activity of etazolate towards cognitive deficits was not disclosed in the art nor suggested by any prior use of this compound.

Withdrawal of the Section 102 rejection of claims 13 and 14 over Ikhlef et al. is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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